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Prevention, screening, assessing and managing of non-adherent behaviour in people with rheumatic and musculoskeletal diseases

systematic reviews informing the 2020 EULAR points to consider

Ritschl, Valentin; Stamm, Tanja A; Aletaha, Daniel; Bijlsma, Johannes W J; Böhm, Peter; Dragoi, Razvan; Dures, Emma; Estévez-López, Fernando; Gossec, Laure; Iagnocco, Annamaria; Negrón, José B; Nudel, Michal; Marques, Andréa; Moholt, Ellen; Skrubbeltrang, Conni; Van den Bemt, Bart; Viktil, Kirsten; Voshaar, Marieke; Carmona, Loreto; de Thurah, Annette

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

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Original research

Prevention, screening, assessing and managing of non-adherent behaviour in people with rheumatic and musculoskeletal diseases: systematic reviews informing the 2020 EULAR points to consider

Valentin Ritschl ¹ Tanja A Stamm ¹ Daniel Aletaha ²
 Johannes W J Bijlsma ³ Peter Böhm ⁴ Razvan Dragoi ⁵ Emma Dures ^{6,7}
 Fernando Estévez-López ⁸ Laure Gossec ^{9,10} Annamaria Iagnocco ¹¹
 José B Negrón ¹² Michal Nudel ¹³ Andréa Marques ¹⁴ Ellen Moholt ¹⁵
 Conni Skrubbeltrang ¹⁶ Bart Van den Bemt ^{17,18} Kirsten Viktil ^{19,20}
 Marieke Voshaar ²¹ Loreto Carmona ²² Annette de Thurah ^{23,24}

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For numbered affiliations see end of article.

Correspondence to

Tanja A Stamm; tanja.stamm@meduniwien.ac.at

ABSTRACT

Objective To analyse how non-adherence to prescribed treatments might be prevented, screened, assessed and managed in people with rheumatic and musculoskeletal diseases (RMDs).

Methods An overview of systematic reviews (SR) was performed in four bibliographic databases. Research questions focused on: (1) effective interventions or strategies, (2) associated factors, (3) impact of shared decision making and effective communication, (4) practical things to prevent non-adherence, (5) effect of non-adherence on outcome, (6) screening and assessment tools and (7) responsible healthcare providers. The methodological quality of the reviews was assessed using AMSTAR-2. The qualitative synthesis focused on results and on the level of evidence attained from the studies included in the reviews.

Results After reviewing 9908 titles, the overview included 38 SR on medication, 29 on non-pharmacological interventions and 28 on assessment. Content and quality of the included SR was very heterogeneous. The number of factors that may influence adherence exceed 700. Among 53 intervention studies, 54.7% showed a small statistically significant effect on adherence, and all three multicomponent interventions, including different modes of patient education and delivered by a variety of healthcare providers, showed a positive result in adherence to medication. No single assessment provided a comprehensive measure of adherence to either medication or exercise.

Conclusions The results underscore the complexity of non-adherence, its changing pattern and dependence on multi-level factors, the need to involve all stakeholders in all steps, the absence of a gold standard for screening and the requirement of multi-component interventions to manage it.

Key messages

What is already known about this subject?

► Non-adherent behaviour is common among people with chronic diseases; for example, 30–80% of people with rheumatoid arthritis do not adhere to treatment at some point of their disease, potentially leading to more disease activity, unnecessary treatment adaptations, loss of quality of life and increased healthcare costs.

What does this study add?

► Non-adherence is triggered by multiple determinants, many of which are not modifiable, and none of which stands as a sole predictor of possible non-adherent behaviour.
 ► Non-adherence can be assessed by multiple instruments; however, no gold standard exists.
 ► Social factors, healthcare-related factors, disease characteristics, as well as therapy-related factors play a potentially important role in adherence; consequently, multicomponent interventions have proven to be the most effective response to non-adherent behaviours.

How might this impact on clinical practice?

► This systematic review has formed the basis of 2020 EULAR points to consider how to facilitate adherence in people with RMDs.

INTRODUCTION

Thirty per cent to eighty per cent of people with rheumatic and musculoskeletal diseases (RMDs) do not follow the prescribed treatment plan. This non-adherent behaviour has a negative impact on pharmacological and/or

non-pharmacological interventions and keeping appointments of follow-up visits.^{1–5} Moreover, being non-adherent is associated with worse clinical outcomes, such as increased risk of cardiovascular disease, decreased functioning and loss of health-related quality of life.^{2–7} Strategies to prevent and/or manage non-adherence are thus essential to achieve an optimal disease outcome.^{4 6 7} Many EULAR recommendations for the management of specific RMDs highlight the importance of adherence to achieve the desired effect of interventions.^{8–11} However, these recommendations do not orient healthcare providers on how to work collaboratively with the patients to support them to adhere to their treatment plans.

A EULAR taskforce was formed to focus on non-adherence across RMDs. Non-adherence affects most types of RMDs and interventions; moreover, it is a complex behaviour that concerns all healthcare providers in rheumatology. An example of the complexity is the influence of a social context. Therefore, successful interventions depend not only on the capability and motivation of the individual patient, but also on contextual factors such as the capability and motivation of, for instance, a spouse or a caregiver.¹² To facilitate a multidisciplinary, multifaceted approach to support adherent behaviour in people with RMDs, taking all these factors into account, the taskforce set out to identify and critically appraise evidence for preventing, screening, assessing and managing non-adherence.

METHODS

We performed a systematic review of systematic reviews (SR) following the guidelines of the Cochrane Collaboration,¹³ and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.¹⁴ According to the EULAR Standard Operating Procedures,¹⁵ an international expert task force was formed, including people with RMDs and representatives from relevant healthcare-provider groups: nurses, occupational therapists, psychologists, physiotherapists, pharmacists and rheumatologists. The task force developed and formulated the following clinical questions with the aim of covering the entire therapeutic process: (1) What strategies are efficacious in facilitating adherent behaviour? (2) What are the factors (barriers, facilitators and so on) that need to be considered to minimise or reduce non-adherence? (3) What is the impact of shared decision making (SDM) and of effective communication on non-adherence? (4) What are the practical things we can do in order to prevent non-adherence? (5) What are the effects of non-adherence on outcome? (6) How is non-adherence screened/detected? (7) Which healthcare providers are responsible for facilitating adherent behaviour? All these questions were translated into their corresponding PICO (Population; Intervention/factor; Comparator; Outcome; in addition, the type of study) formulae (table 1).

Search strategy

We conducted an electronic search of the following databases: Medline (via PubMed), Embase, CINAHL and Cochrane databases, from inception until 12 June 2018. Due to the broad spectrum of the topic, the task force decided to limit the search to the most important/frequent topics, being ‘drug therapy’, ‘exercise’, ‘nutrition’ and ‘visits’. We used comprehensive free text and MeSH synonyms for ‘adherence to drug therapy’, ‘adherence to exercise’, ‘adherence to diet’ and ‘adherence to visits’, plus synonyms of RMDs, with a filter for SR. ‘Exercise’ in this context refers to any physical activity, exercise or training; ‘visits’ mean regular medical check-ups with a healthcare provider. Additionally, a search strategy was developed to capture studies of instruments to assess adherence in RMDs. The electronic search strategies are available as a supplemental file (online supplemental A). We limited the search to reviews in adults and articles published in English during the last 10 years. It was decided by the task force to exclude children and adolescents (below the age of 18) from the literature search, as their non-adherent behaviour differs from that of adults, mainly on its great reliance on social support of caregivers.¹²

Study selection

The selection criteria of the studies were different for each of the questions and based on their specific PICO (table 1). Two authors (JBN, AdT) independently assessed the electronic search results for each of the questions. They first screened studies by title and then by abstract. When an article title seemed relevant, the abstract was reviewed for eligibility. If there was any doubt, the full text of the article was retrieved and appraised for possible inclusion. Any differences among the two authors were discussed, and if necessary, a third author (LC) was referred to for arbitration. A reason for exclusion was recorded in all cases if the article was not eligible or excluded (online supplementals B–H).

Risk of bias assessment

Cochrane SR were included without further critical appraisal, as it is mandatory for them to follow rigorous methods.¹³ Any other SR underwent a critical appraisal by one author (VR), supervised by the methodologist (AdT), using the AMSTAR 2 tool.¹⁶ The quality and risk of bias of the original studies were obtained directly from the published SR.

Data extraction and synthesis

Three authors (VR, LC and JBN) extracted the data, supervised by the methodologist (AdT). Data included design, population, intervention or factors studied, comparator (if applicable), outcome(s) measured and results.

The results were synthesised qualitatively for each clinical question. No meta-analysis was intended, as the heterogeneity across studies in terms of population,

Table 1 The clinical questions/PICOs addressed in this review. Questions #1 to #5 and #7 were answered on the basis of the articles identified in the first literature search. An additional literature search was performed to answer question #6 (online supplemental A)

#	Clinical question	P	I	C	O
1	What strategies are efficacious in facilitating adherent behaviour?	Adults with any RMD	Any intervention or strategy managing non-adherence	SoC or other strategy	Adherence
2	What are the factors (barriers, facilitators) that need to be considered to minimise or reduce non-adherence?		–	–	Barriers and facilitators of adherence
3	What is the impact of SDM and of effective communication on non-adherence?		SDM and effective communication	–	Adherence
4	What are the practical things we can do in order to prevent non-adherence?		Effective interventions or strategies for enhancing adherence	–	Components of intervention
5	What are the effects of non-adherence on outcome?		(Non-)Adherence	–	Outcome: Treatment effect, Function Disability Structural damage Fracture
6	How is non-adherence screened/detected?		Measurement or screening instruments	–	Screening performance Metric properties
7	Which healthcare providers are responsible for managing non-adherence?		Effective interventions or strategies for enhancing adherence	–	Health-care provider performing intervention

PICO, Population; Intervention/factor; Comparator; Outcome; RMD, rheumatic and musculoskeletal disease; SoC, standard of care; SDM, shared decision making.

interventions and outcomes measured precluded such quantitative approach.

RESULTS

The search strategies yielded 9908 records, of which 3600 were related to adherence to medication, 2357 to exercise, 542 to diet, 1872 to visits and 1537 to the screening or assessment of adherence in RMD. After exclusion of duplicates and title/abstract screening, 95 studies were analysed in full text. According to the different inclusion and exclusion criteria, a different number of papers was included for each PICO. The PRISMA flowchart of the study selection is depicted in [figure 1](#).

Risk of bias of the included SR

The quality of the SR was in general low. The quality of the included individual studies is described for each clinical question (online supplementals B–H).

Population of the included studies

There are more than 200 RMDs;¹⁷ however, the studies found in the reviews dealing with non-adherence and RMDs contained only eight different RMDs: rheumatoid arthritis (RA), osteoporosis, systemic lupus erythematosus (SLE), osteoarthritis (OA), gout, spondyloarthritis, psoriatic arthritis and low back pain.

Clinical question 1: what strategies are efficacious in facilitating adherent behaviour?

We included studies examining interventions aiming at improving non-adherent behaviour in comparison to standard care or other interventions. We searched for articles regarding medication/exercise adherence, adherence to diet/visits (See full report in online supplemental_B_PICO_1).

The screening by title and abstract yielded 38 studies to be appraised in full-text, of which four were SR on interventions to improve adherence to medication,^{15 18–20} eight SR on adherence to exercise^{21–28} and one on adherence to scheduled visits.²⁹ We did not find any reviews regarding adherence to diet specifically in RMDs. In total, these reviews included 17 original studies on adherence to medication,^{30–46} 33 on exercise or physical activity^{33 47–79} and three on visits.^{80–82}

Due to the variety of interventions, we classified them into six categories: (1) educational (enhance patient knowledge), (2) behavioural (providing incentives for medication taking), (3) cognitive behavioural (altering thinking patterns) and (4) multicomponent intervention (multiple strategies used).^{18 83} For exercise, two categories were added: (5) motivational (increasing motivation) and (6) supervised/class-based exercises. Interventions that did not fit into these categories were classified as ‘others’, such as

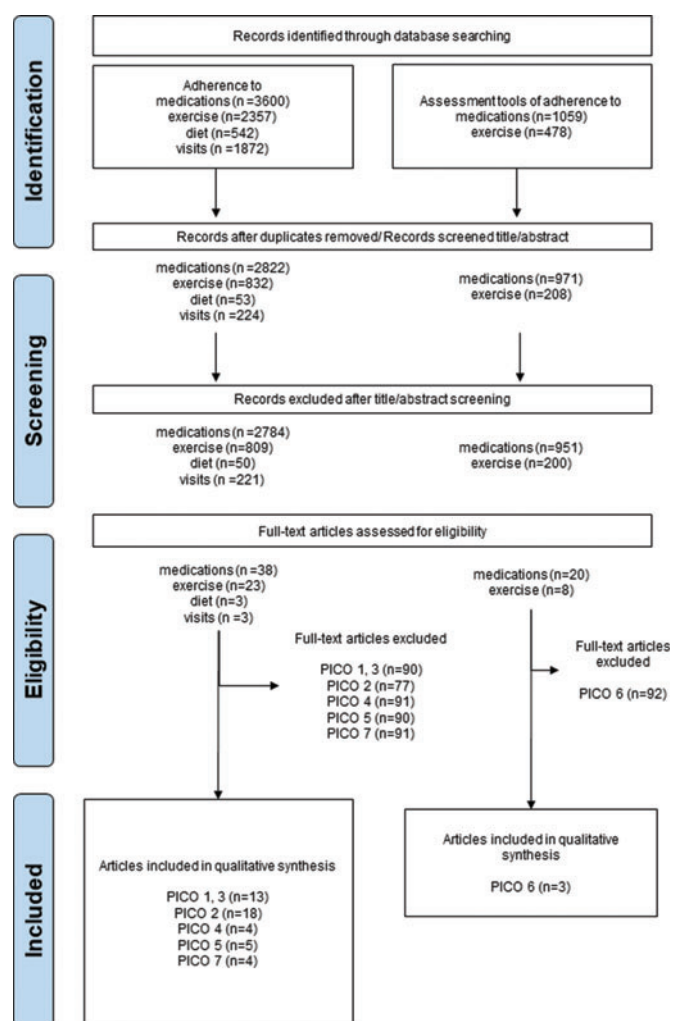


Figure 1 PRISMA flow diagram. This flow chart shows the study selection for the search strategies and PICOs. As the PICOs had different exclusion and inclusion criteria, the number of excluded and included articles varies. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PICO, Population; Intervention/factor; Comparator; Outcome.

computer-assisted video instructions (to conventional education)⁷⁷ or cost-free programmes compared to fee-based-programmes.⁷⁶

The results were very heterogeneous in terms of diagnosis, interventions, outcome measures (see clinical question 6) and in regard of effectiveness. More than half of all interventions (n=29, 54.7%) included an educational or behavioural approach. Among the 53 studies included in the SR, 29 (54.7%) documented a small statistically significant effect on adherence. Among the remaining studies, six documented an unclear effect, and in 18 studies, no statistical significance was reached. All three multicomponent interventions showed a positive result in adherence to medication. Studies using cognitive behavioural or motivational approaches showed positive results;

however, only three such studies were included in the SR (table 2).

Clinical question 2: what are the factors (barriers, facilitators) that need to be considered to minimise or reduce non-adherence?

We included SR, specifically aiming at describing barriers or facilitators of adherence to medication or to exercise or physical activity (See full report in online supplemental_C_PICO_2). After excluding narrative reviews, expert opinions and reviews on interventions, 15 SR on factors affecting medication non-adherence^{84–98} and four on exercise^{99–102} were included.

Determinants for medication non-adherence are multifaceted.^{84–98} Some factors may change over time and can act both as a cause and as a consequence of non-adherence. For example, clinical improvement seems to increase non-adherence behaviour. This may lead to worsening of symptoms which may urge patients to become more adherent.⁹⁰

Some factors are not modifiable, for example, age and gender, and none is considered an isolated predictor of non-adherence.^{84 87 88} In their SR, Kardas & Lewek identified 771 individual factors related to medication non-adherence, covering 19 different diseases.⁹⁰ They grouped their results into 40 clusters, mapped into the five WHO categories: socio-economic factors, healthcare team and system-related factors, condition-related factors, therapy-related factors, patient-related factors.¹⁰³

Only four reviews addressed factors related to adherence to exercise.^{99–102} Similar to adherence to medication, adherence to exercise or physical activity is affected by multiple determinants. A SR, including low risk of bias studies, demonstrated that knowledge, skills, social or professional identity, beliefs about capabilities, optimism, beliefs about consequences and reinforcement influence adherence behaviour to exercise among patients with hip or knee OA.⁹⁹ The Cochrane mixed methods review by Hurley & Dickson concluded that (1) better information and advice about the safety and value of exercise, (2) exercise tailored to individuals' preferences, abilities and needs and (3) verbalisation of inappropriate health beliefs and better support, reduced non-adherent behaviour to exercise.¹⁰⁰

Clinical question 3: what is the impact of shared decision making (SDM) and of effective communication on non-adherence?

To answer clinical question 3, all interventions included in the SR for PICO 1 were reviewed in detail, specifically seeking components of effective communication or SDM. Although no evidence was found specifically on the impact of SDM or effective communication on non-adherence in RMDs (See full report in online supplemental_D_PICO_3), the results to the next clinical question were very much related.

Table 2 Summary of the included studies, PICO 1

	Dx	Edu	Beh	CBT	Mot	Sup	MCo	Oth
Medication	RA	3+/3–	1+/1–	1+			2+	1~
	SLE	1+	1–					
	Psoriasis						1+	
	OP							1~/1–
	Total	4+/3–	1+/2–	1+			3+	2~/1–
Exercise	OA	2+/4–	3–		1+	2+/1–		3+/2–
	RA	2+	3+/2–				3~	
	Mixed	1+	1+					
	CBP		1~		1+		1+	
	Total	5+/4–	4+/1~/5–		2+	2+/1–	1+/3~	3+/2–
Visits	RA							3+
	SLE							
	Total							3+

Beh, behavioural interventions; CBP, chronic back pain; CBT, cognitive-behavioural therapy; Dx, diagnosis; Edu, educational interventions; MCo, multicomponent interventions; Mot, motivational interventions; OA, osteoarthritis; OP, osteoporosis; Oth, other interventions; PICO, Population; Intervention/factor; Comparator; Outcome; RA, rheumatoid arthritis; Sup, supervised exercise; SLE, systemic lupus erythematosus. The numbers indicate the count of the studies. Numbers followed with a '+' indicate significant increase in adherent behaviour, '-' means no increase in adherent behaviour and '~' means unclear results.

Clinical question 4: what are the practical things we can do in order to prevent non-adherence?

To better guide HCP in clinical routine, to better support patients in their adherence, we searched studies for useful and effective 'everyday' ideas and suggestions. All interventions proven effective in the SR of PICO 1 were reviewed in detail. The individual components of the effective interventions were collected and summarised (See full report in online supplement_E_PICO_4).

One important practical aspect was patient education (PE), defined, according to the EULAR recommendations, as a 'planned interactive learning process designed to support and enable people to manage their life with inflammatory arthritis and optimise their health and well-being'.¹⁰ Five SR including 51 studies explored the association between (different) modes of PE and adherence in people with RMDs. Fifteen studies had a positive impact on non-adherence, nine of which were studies on medication,^{30 31 36 37 39–42 104} and six on exercise.^{50 52 66 70 79 105} Nine studies showed a positive, but not statistically significant effect; five studies on medication,^{32 43 45 105 106} and four on exercise.^{53 55 61 75} The PE modes to enhance adherence to medication varied greatly: daily text messages to provide reminders and education,⁴¹ information and written materials,^{31 42} chart visualisation of disease progression,³⁷ discussion of patient-reported outcome measures (=PROMs),⁴² counselling and advice,⁴⁵ motivational interview.^{43 106} The PE interventions for adherence to exercise also were varied: consultations,^{52 55 75 105} motivational approaches,⁷⁰ physical activity advice⁵⁰ and verbal (recorded tapes) and visualised (videos) cues to prompt correct performance of exercise.⁵³ Regarding the content of the PE to improve

medication adherence, this included information about drugs,^{31 36} disease process,^{31 36} physical exercise,³¹ joint protection,^{31 42} pain control,^{31 42} coping strategies³¹ and lifestyle changes.^{36 42} The studies which focused on PE to improve adherence to exercise include additional information about physical exercise, endurance activities (walking, swimming, bicycling), advice on energy conservation and joint protection.¹⁰⁵ The mode of delivering PE was diverse: verbally, either by face to face,³¹ or by telephone,³⁰ written, as in leaflets,³¹ or in text messages,^{39 41} and visualised, as in charts.³⁷

In addition to PE, other practical things to prevent non-adherence were mentioned in the studies. Patients should be given the ability to express questions and doubts.³⁶ Physicians and health professionals in rheumatology (HPRs) should review the plans and strategies and provide feedback and solve any doubts.¹⁰⁴ Adherence behaviour is supported by interventions that are individualised or tailored according to predefined goals and preferences of the patient.^{40 50 66} Effective interventions included the encouragement of patients to set realistic goals in planning their treatment regimens, and the training of patients in proper execution of physical exercises.¹⁰⁵ They also included photos displaying exercises and explanatory written information,⁷⁹ and discussed issues of non-adherence, possible alternatives and solutions with the patient¹⁰⁵ (table 3). Following the perceptions of healthcare providers, organisational aspects, such as limited consultation time, were the main obstacles to effective communication.⁵² Social support^{58 60 62 63 67 68} was used to support adherence to physical activity and exercises. Reminders did not increase the use of hydroxychloroquine but to follow up visits.³⁹

Table 3 Summary of practical things we can do in order to prevent non-adherence**Medication adherence**

Practical thing we can do	Examples/descriptions
Education/information should include information about	<ul style="list-style-type: none"> ▶ Drugs ▶ Disease process ▶ Physical exercise ▶ Joint protection ▶ Pain control ▶ Coping strategies ▶ Lifestyle changes
Education/information can be delivered	<ul style="list-style-type: none"> ▶ Verbally (face to face or by telephone) ▶ Written (leaflets or text messages) ▶ Visualised in charts
Cueing	For example: pairing medication taking with an established behaviour such as brushing teeth
Monitoring	For example: using a calendar to track medication taking
Positive reinforcement	For example: praising and rewarding with tokens that are exchanged for special privileges
Possibility to express questions and doubts	Patients should have the possibility to express questions and doubts
Review of plans/strategies	Physician and other health professionals should review the plans/strategies and give feedback/answers
Individualised/tailored treatment	Individualised/tailored treatment according to patient preferences and goals

Exercise adherence

Practical thing we can do	Examples/descriptions
More consults/time	Overcome the constraint of consultation time
Use psychosocial factors relevant for the motivational approach as proxy efficacy	Proxy efficacy refers to patients' confidence in their therapists' ability to function effectively on their behalf
Education/information should include information about	<ul style="list-style-type: none"> ▶ Physical exercises ▶ Endurance activities (walking, swimming, bicycling) ▶ Advice on energy conservation ▶ Joint protection
Discuss problems	Discuss problems regarding exercise adherence and offer solutions
Encourage patients to take responsibility	For example: to plan their treatment regimens, discuss intentions and help recasting unrealistic plans
Individualised/tailored treatment	Individualised physical activity advice and tailored graded exercise programme according to the preferences and goals of the patient.
Train in proper execution of physical exercises	Photos displaying these exercises and explanatory written information

Clinical question 5: what are the effects of non-adherence on outcome?

To answer clinical question 5, all individual studies included in the first SR were reviewed. Studies were included if, besides adherence, other clinical outcomes, such as disease activity or patient's perspective, were measured and the association with adherence analysed (See full report in online supplemental_F_PICO_5).

None of the included studies specifically focused or analysed the impact of non-adherent behaviour on health outcomes. However, in some studies, differences in clinical outcomes were seen between groups of patients with high adherence scores compared with less adherent patients. The association was evident in terms of improvement in disease severity,^{37 39 41 42} pain,^{37 41 42 79} functional status,^{37 40–42 70 79} fatigue,⁴⁰ depression⁴⁰, quality of life^{37 41 42 70} and physical activity levels.^{50 52 66 105}

Clinical question 6: how is non-adherence screened/detected?

For this question, the type of studies targeted were validation studies of questions, questionnaires, tailored assessments and other kinds of measures to assess and/or screen non-adherence in people with RMDs (See full report in online supplemental_G_PICO_6). While conducting our review, a SR of tools to assess adherence to medication, which passed our AMSTAR2 quality check, was presented at the Euler Congress.¹⁰⁷ It included 242 validation studies, and identified four questionnaires (patient-reported outcome measures) that have been used to measure non-adherence to medication in inflammatory arthritis: the Compliance Questionnaire in Rheumatology (CQR),¹⁰⁸ the Medication Adherence Report Scale (MARS),¹⁰⁹ the Morisky Medication Adherence Scale (MMAS)^{110 111} and the Medication Adherence Self-report Inventory (MASRI).¹¹² The most commonly used measurement is the MMAS, although it is subject to a fee

and not fully validated in rheumatology. The CQR and MASRI questionnaires are the most widely validated in rheumatology; however, the CQR is an 18-item questionnaire, and hence, most suitable for research purposes. Within rheumatology, the MASRI has only been used in SLE.¹¹³ The authors of the SR concluded that up to date, a simple, reliable and valid questionnaire to assess medication adherence in daily clinical practice is not available.

We then focused our SR on measurements of adherence to exercise. Three SR covering 162 individual studies and describing 76 ways of measuring non-adherence to prescribed exercise interventions were identified.^{114–116} Currently, there is no gold standard measurement of adherence to exercise. The existing ones can be categorised as (1) (self-developed) questionnaires, scales, interviews or surveys (eg, asking for exercise-frequencies)¹¹⁷; (2) diaries or logbooks (eg, counting frequencies)¹¹⁸ and (3) other type of assessments (eg, different types of monitors and devices, such as StepWatch Activity Monitor (SAM)).¹¹⁵ The majority of tools do not have a proper description or testing of their metric properties available, except for the Heart Failure Compliance Questionnaire,¹¹⁹ the Adherence to Exercise Scale for Older Patients (AESOP)¹²⁰ and The Problematic Experiences of Therapy Scale¹²¹; however, none of these scales are specifically developed or tested among people with inflammatory arthritis.

Clinical question 7: which healthcare providers are responsible for managing non-adherence?

To answer clinical question 7, all interventions in the included SR that showed a positive effect were reviewed in detail (See full report in online supplemental_H_PICO_7). The healthcare providers delivering these effective interventions were ranked by frequency, rheumatologists or other physicians,^{37 42 52 79 105} nurses,^{31 104} pharmacists,^{30 36} physiotherapists,^{66 70} therapists,⁴⁰ exercise physiologist⁵⁰ and patient educators.⁴³

DISCUSSION

This overview of SR allowed us to answer clinical questions regarding adherence in RMDs. Despite the lack of assessment standards and evidence for interventions, non-adherence is a behaviour that is assumed to lead to a worse outcome and should therefore be addressed.

The findings of these reviews informed a EULAR task force developing the 2020 EULAR points to consider for the prevention, screening, assessment and management of non-adherence in people with RMDs. The intention to use this type of review compared to others was to examine only the highest level of evidence. A strength of this type of review is that it provides an overall picture of findings. Therefore, a SR of SR is an ideal means to provide rapid evidence synthesis for clinical decision-makers with the evidence they need.^{122 123} A challenge in doing such overview is the risk of including data from individual studies more than once. This could happen if studies

are included in two or more reviews. This would result in a misleading estimate.^{122 123} To overcome this obstacle, once we selected the reviews we analysed the results of the individual studies, including them only once.

The PICO/clinical questions formulated in the first task-force meeting aimed to cover the entire therapeutic process. The questions focused on prevention, screening, assessment and management of non-adherent behaviour. We only included adults who are independent of caregivers. We believe that the inclusion of caregivers requires a comprehensive extension of the scope and search. Children and older people or people with cognitive limitation who are dependent on a guardian/carer need special attention in terms of non-adherence.¹² For this group of people, non-adherence behaviour differs from that of adults, mainly due to the great reliance on social support of caregivers.¹²

Our main message from this review is that adherence is very complex in nature, and thus that there is no single explanation for non-adherence. This means, there is no single factor for being non-adherent, but multiple factors influencing each other. Nevertheless, most studies have not considered the individual factors leading to non-adherence, and consequently used one and the same approach for all patients. This might be one of the reasons why especially tailored multi-component strategies are more efficacious compared to single interventions. However, to be evaluated, these tailored multi-component strategies require complex methods, very large sample sizes to avoid noise and solid outcome measures, which do not seem to be available.

We did not find any review that examined the impact of SDM or effective communication on (non-)adherence. Furthermore, we did not find a clear definition of 'effective communication' in healthcare. Instead of 'effective communication' we found 'patient education/information' to be similar to the term 'effective communication' (as it was understood from the task force) and an important tool to support patients in their adherent behaviour. With regard to SDM, we found that patient-tailored approaches are more effective than non-tailored approaches. However, since the results did not answer question 3, we moved these findings to question 4.

In accordance to the very complex nature of non-adherence, there is no gold-standard for screening or assessing it. Moreover, when adherence is discussed directly by a healthcare provider, there will be a risk of socially desirable answers. Healthcare providers have to take this into account, when they are evaluating (non-)adherence to a treatment regimen.

We acknowledge that our review has certain limitations. Most of the SR and studies included focused only on osteoarthritis, gout, osteoporosis and RA. Other types of inflammatory arthritis are under-represented and this may have introduced a bias of the results. Most of the SR and studies had adherence to medication or exercise as outcome. Adherence to diet and clinical visits was under-represented in this review. Further, the data extraction

was performed by only one researcher. A disadvantage of using a review of reviews is that there may be studies in recent years, which were not included in any review, and therefore are not included in this overview as well. In addition, SR of SR should not only summarise the evidence, but should also include a resynthesis of the data.^{122 123} Due to the high heterogeneity, we were not able to perform a meta-analysis across the different reviews. We have focused solely on the effectiveness of interventions to support adherent behaviour in people with RMDs. Feasibility, cost-effectiveness and other factors were not further considered. Healthcare providers have to take in mind that the results of this review are based on study context, which can be different to daily practice. Finally, all studies suffered from some methodological limitations that impacted the level of evidence.

In conclusion, the results underscore the complexity of non-adherence, its changing pattern and dependence on multi-level factors. As agreement is part of the definition of adherence in the sense, that people with RMDs have to agree to the treatment plan, the need to involve all stakeholders, meaning healthcare providers and people with RMDs in all phases of treatment (prevention, screening, assessment and management), became obvious. The absence of a gold standard for screening and assessing non-adherence, and the requirement of multi-component interventions to manage it, sets an agenda for future research.

Author affiliations

¹Section for Outcomes Research, Medical University of Vienna, Wien, Austria

²Division of Rheumatology, Medical University of Vienna, Wien, Austria

³Rheumatology, UMC Utrecht, Utrecht, Netherlands

⁴Deutsche Rheuma-Liga Bundesverband e.V., Bonn, Germany

⁵University of Medicine and Pharmacy Victor Babes Timisoara, Timisoara, Romania

⁶University of the West of England Bristol, Bristol, UK

⁷Academic Rheumatology, Bristol Royal Infirmary, Bristol, UK

⁸Erasmus MC University Medical Centre, Rotterdam, Netherlands

⁹Institut Pierre Louis d'Epidémiologie et de Santé Publique, INSERM, Sorbonne Université, Paris, France

¹⁰APHP, Rheumatology Department, Hôpital Universitaire Pitié Salpêtrière, Paris, France

¹¹Università Degli Studi di Torino, Torino, Italy

¹²Instituto de Investigación Social y Sanitaria, Puerto Rico

¹³Mifrakim Tz'eirim, Haifa, Israel

¹⁴Centro Hospitalar e Universitário de Coimbra, Health Sciences Research Unit: Nursing, UICISA-E, Coimbra, Portugal

¹⁵Diakonhjemmet Hospital, Division of Rheumatology and Research, Oslo, Norway

¹⁶Aalborg Universitetshospital, Aalborg, Denmark

¹⁷Pharmacy, Sint Maartenskliniek, Nijmegen, Netherlands

¹⁸Radboud University Medical Centre, Nijmegen, Netherlands

¹⁹University of Oslo, Oslo, Norway

²⁰Diakonhjemmet Hospital Pharmacy, Oslo, Norway

²¹University of Twente, Enschede, Netherlands

²²Instituto de Salud Musculoesquelética (Inmusc), Madrid, Spain

²³Rheumatology, Aarhus University Hospital, Århus N, Denmark

²⁴Clinical Medicine, Aarhus University, Aarhus, Denmark

Twitter Fernando Estévez-López @FerEstevezLope1 and José B Negrón @negrónjb.

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ORCID iDs

Valentin Ritschl <http://orcid.org/0000-0001-8763-8215>

Tanja A Stamm <http://orcid.org/0000-0003-3073-7284>

Daniel Aletaha <http://orcid.org/0000-0003-2108-0030>

Johannes W J Bijlsma <http://orcid.org/0000-0002-0128-8451>

Peter Böhm <http://orcid.org/0000-0002-7186-1997>

Razvan Dragoi <http://orcid.org/0000-0002-3991-7583>

Emma Dures <http://orcid.org/0000-0002-6674-8607>

Fernando Estévez-López <http://orcid.org/0000-0003-2960-4142>

Laure Gossec <http://orcid.org/0000-0002-4528-310X>

Annamaria Iagnocco <http://orcid.org/0000-0001-5592-724X>

José B Negrón <http://orcid.org/0000-0003-4659-5508>

Andréa Marques <http://orcid.org/0000-0002-2026-9926>

Conni Skrubbeltrang <http://orcid.org/0000-0002-7478-8422>

Bart Van den Bemt <http://orcid.org/0000-0002-8560-9514>

Kirsten Viktil <http://orcid.org/0000-0003-2361-5107>

Marieke Voshaar <http://orcid.org/0000-0002-4161-0126>

Loreto Carmona <http://orcid.org/0000-0002-4401-2551>

Annette de Thurah <http://orcid.org/0000-0003-0103-4328>

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